REMARKS

Applicant is in receipt of notice of non-compliant amendment under 37 CFR 1.121. Applicant has addressed the issue and believes that the claims are in compliance. Applicant appreciates the Examiner's time during the interview of October 26, 2005. Reconsideration and further examination of this application is hereby requested. Claims 1, 6-9, 13 and 19 are amended, claim 21 is newly added and claims 1-21 are currently pending in the application. No new matter has been added.

35 U.S.C. 103(a)

The Examiner has rejected claims 1-8, 14-20 under 35 U.S.C. 103(a) as obvious over Moon (2003/0092195). Applicant traverses the Examiner's rejection in light of Moon for the following reasons.

Applicant has amended claim 1 wherein the distance from the capillary tip to the target is between .25 to .5 mm. The distance is supported by the disclosure dated prior to September 17, 1998 and referenced in the Declaration filed March 22, 2005.

Amended claim 1 is patentable over Moon because Moon teaches ionization of a sample and detection of the ions in the sample at a mass spectrometer "target" detector. The electrospray sample enters an ion sampling orifice on its way to the "target" detector of the mass spectrometer. The ion sampling orifice is not the "target" but merely a point in space that the sample passes on its passage to the "target". Further, the distance between the capillary tip and the "target" is not 2 mm or less as posited by the Examiner but instead the distance to the "target" is greater than 2mm given the distance to the "target" is equal to

"a + b" where "a" is the distance between the capillary tip and the ion sampling orifice and "b" is the distance between the ion sampling orifice and the "target". Therefore, paragraphs [0036]-[0040] of Moon do not teach the distance between the tip of the capillary and the target to be within the range claimed by the Applicant as the target is not the orifice.

Paragraphs [0036]-[0040] read as follows:

> [0036] Because the electrospray device is manufactured using reactive-ion etching and other standard semiconductor processing techniques, the dimensions of such a device can be very small, for example, as small as 2 μm inner diameter and 5 μm outer diameter. Thus, a nozzle having, for example, 5 μm inner diameter and 250 μm in height only has a volume of 4.9 pL (picoliter). In contrast, an electrospray device from the flat edge of a glass microchip would introduce additional dead volume of 12 nL compared to the volume of a separation channel of 19.8 nL thereby allowing remixing of the fluid components and undoing the separation done by the separation channel. The micrometer-scale dimensions of the electrospray device minimizes the dead volume and thereby increases efficiency and analysis sensitivity.
>
> [0037] The electrospray device of the present invention provides for the efficient and effective formation of an electrospray. By providing an electrospray surface from which the fluid is ejected with dimensions on the order of micrometers, the electrospray device limits the voltage required to generate a Taylor cone as the voltage is dependent upon the nozzle diameter, surface tension of the fluid and the distance of the nozzle from the extracting electrode. The nozzle of the electrospray device provides the physical asperity on the order of micrometers on which a large electric field is concentrated. Further, the electrospray device may provide additional electrode(s) on the ejecting surface to which electric potential(s) may be applied and controlled independent of the electric potentials of the fluid and the extracting electrode in order to advantageously modify and optimize the electric field. The combination of the nozzle and the additional electrode(s) thus enhance the electric field between the nozzle and the extracting electrode. The large electric field, on the order of 10^6 V/m or greater and generated by the potential difference between the fluid and extracting electrode, is thus applied directly to the fluidic cone rather than uniformly distributed in space.
>
> [0038] The microchip-based electrospray ionization device of the present invention provides minimal extra-column dispersion as a result of a reduction in the extra-column volume and provides efficient, reproducible, reliable and rugged formation of an electrospray. The design of the ionization device is also robust such that the electrospray device can be readily mass-produced in a cost-effective, high-yielding process.

[0039] In operation, a conductive or partly conductive liquid sample is introduced into the channel through the entrance orifice on the injection surface. The liquid sample and nozzle are held at the potential voltage applied to the fluid, either by means of a wire within the fluid delivery channel to the electrospray device or by means of an electrode formed on the injection surface isolated from the surrounding surface region and from the substrate. The electric field strength at the tip of the nozzle is enhanced by the application of a voltage to the substrate and/or the ejection surface, preferably approximately less than one-half of the voltage applied to the fluid. Thus, by the independent control of the fluid/nozzle and substrate/ejection surface voltages, the electrospray device of the present invention allows the optimization of the electric field lines emanating from the nozzle. Further, when the electrospray device is interfaced downstream with a mass spectrometry device, the independent control of the fluid/nozzle and substrate/ejection surface voltages also allows for the direction and optimization of the electrospray into an acceptance region of the mass spectrometry device.

[0040] The electrospray device of the present invention may be placed 1-2 mm or up to 10 mm from the orifice of an API mass spectrometer to establish a stable nanoelectrospray at flow rates as low as 20 nL/min with a voltage of, for example, 700 V applied to the nozzle and 0-350 V applied to the substrate and/or the planar ejection surface of the silicon microchip.

It is clear from the passage cited by the Examiner that the "orifice" is not the "target" but merely an opening to a vacuum chamber wherein the droplets evaporate along the flight path towards the detection "target" of the Mass Spectrometer. In this context, the invention of Moon is focused on confining the electric field using ring-electrodes (paragraph [0036]) such that (most) preferably all of the droplets from the spray fly unhampered through the orifice thereby avoiding deposition onto the orifice surface which obviously may result in discharging and unstable straying. The orifice in Moon has a small diameter in order to achieve the required vacuum.

Further more, in paragraph [0040], Moon states that a voltage of 0-350 V may be applied to the substrate and/or planar ejection surface of the silicon microchip. However as indicated in picture 24C, "substrate" refers to the ring electrode 120 (connected to

Vsubstrate) around the nozzle, which lies on top of the planar ejection surface 112 as is shown in Figure 2 and explained in paragraph [0080].

For clarity: in draft 24 C, the text "mass spectrometer" used by Moon is in fact the "vacuum chamber of the mass spectrometer".

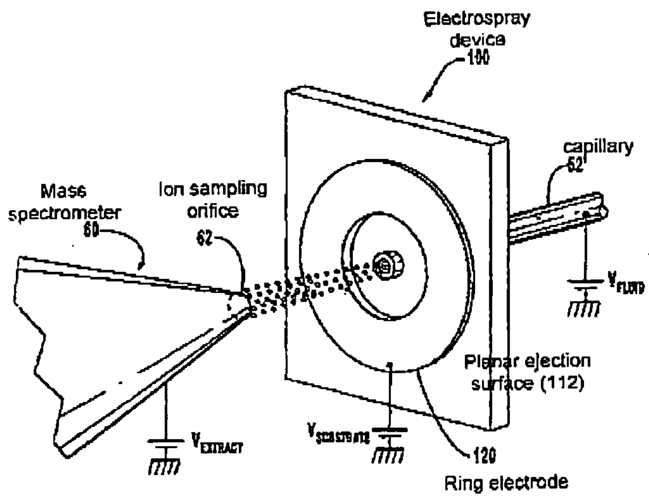
Electrospray device
100
capillary
52
Mass spectrometer
60
Ion sampling orifice
62
V_{FLUID}
Planar election surface (112)
$V_{EXTRACT}$
$V_{SUBSTRATE}$
120
Ring electrode

FIG. 24C

The substrate is not the "target". Further, the ring electrode would cause discharge of the electrospray in light of the conducting film thereon. Therefore, Moon does not teach a method of electrospray transfer between the tip of a capillary and the target but teaches a method of spraying liquid droplets through an ion sampling orifice where the distance between the tip and ion sampling orifice is in the range of between 1 to 10 mm allowing the sprayed droplets to pass through the orifice in an optimal manner.

Further, the only time Moon discusses the distance between the electrospray device and another point of an assay system is in the context of the mass spectrometer device and the orifice of an API mass spectrometer. (See [0026], [0027], [0040], [0085], [0149] and [0227]). Moon does not discuss a distance between the nozzles 330 and the receiving wells 334 illustrated in figure 23B which are referenced in paragraphs [0144]-[0146].

Since deposition of a sample is not ionization of a sample it is improper to borough the dimensions and geometry taught by Moon for the mass spectrometer application and apply those teachings to electrospray deposition on a plate because one of ordinary skill in the art would not expect the same results between the two systems.

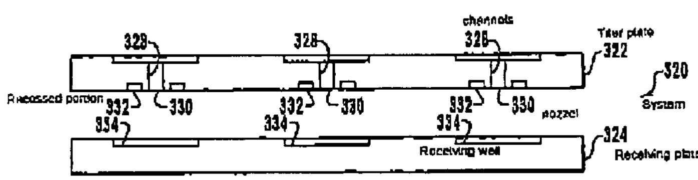
channels
Titer plate
328
328
328
322
320
System
Recessed portion
332
330
332
330
332
330
334
334
334
324
Receiving well
Receiving plate

FIG. 23B

Furthermore, Moon is not a valid 103(a) reference because Applicant's embodiments of the inventin as claimed in claim 1 predates the Moon filing date. (See rule 131 Declaration filed March 22, 2005). For the above mentioned reasons claim 1 is patentable over Moon.

Claims 3-20 depend from claim 1 and are patentable for at least the same reasons as cited in support of claim 1.

New claim 21 recites the elements as disclosed by Applicant in a disclosure that predates the Moon reference (see rule 131 Declaration filed March 22, 2005). Therefore Moon is not a valid reference against claim 21. Morozov (6,350,609) does not teach each and every element of claim 21. Therefore, claim 21 is patentable.

The Examiner has rejected claims 9-13, and 15-19 as obvious over Moon in light of Morozov (6,350,609).

Applicant traverses this rejection. Morozov does not teach, suggest or motivate one to combine the electrospray deposition as taught by Morozov with the electrospray sample introduction into the mass spectroscopy orifice of Moon at a distance of 2mm. Morozov does not contemplate, suggest or teach improvements to the deposition process by managing the geometries of the capillary tip size nor the distance between the capillary tip and the target substrate. Morozov clearly contemplates the deposition of the electrospray substance onto the target substrate where the deposits are used to determine the interaction of the deposited substances to other substances. Morozov is silent as to the distance

between the tip of the capillary electrospray device and the substrate. Morozov is also silent as to the geometry of the capillary tip.

Conclusion

For the above reasons, Applicant respectfully submits that the application is in condition for allowance with claims 1-20. If there remain any issues that may be disposed of via a telephonic interview, the Examiner is kindly invited to contact the undersigned at the local exchange given below.

The Commissioner is authorized to charge any necessary fees, and conversely, deposit any credit balance, to Deposit Account No. 13-4213.

Respectfully submitted,

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